

CLAIMS

1. A peptide having, in particular, an antiangiogenic activity, characterized in that it is a cyclized peptide corresponding to the sequence

SEQ ID No 1: $X_1X_2RGDX_3FGX_4X_5LLFIHFX_6IGSX_7HSX_8IX_9$ in which:

- the letters without any numerical index correspond to amino acids defined by the single-letter international code,
- 10 - X_1 is either a G or a GG, the amino-terminal end of which is free, alkylated, acylated, or in particular acetylated, or contains a labeling group, such as the biotinyl group,
- X_2 is either a C, in which case $X_2 = X_4$, the two Cs then being connected by a disulfide bridge, or X_2 is capable of forming a lactam bridge with X_4 , one of X_2 or X_4 being an amino acid bearing an acid group, such as A or D, the other bearing an amino function, such as Q or N,
- 15 - X_3 is either an M motif or a norleucine motif,
- X_5 is either a motif, or a succession of two di-, tri- or tetrapeptide motifs composed of G or a combination of G and of S, such as GG, GGG, GGGG, GGS, GGGG or GGS GGS, or else X_5 is a C motif, the side chain (thiol function) of which serves as a point for covalent bonding with a 3-nitro-2-pyridinesulphenyl group located on the N-terminal end of the next amino acid (L),
- 20 - X_6 is either an R motif or a K motif,
- 30 - X_7 is either an R motif or a K motif,
- X_8 is either an R motif or a K motif,
- X_9 is an aliphatic amino acid (such as G or A), the C-terminal end of which is amidated.

35 2. The peptide as claimed in claim 1, characterized in that it corresponds to the sequence

SEQ ID No 2: GG*CRGDMFG*CGLLFIHFRIGSRHSRIG

(*indicates a disulfide bridge connecting the two C

motifs).

3. The peptide as claimed in claim 1 or 2, characterized in that it is modified compared with the native peptide and has, in particular, an alkylated group at its N-terminal end, and/or in that more amino acids are replaced with one or its/their dextrorotary form (_Daa), and/or in that it contains one or more peptide bonds so as to form bioisosters, for example the reduction of an amide bridge to -CH₂NH-, or a retro-inverso reaction.

4. The peptide as claimed in claim 2, in which the RGD motif is exposed via a disulfide bridge between two cysteines, in particular the peptides of sequences SEQ ID No 3 to 10:

SEQ ID No 3: GG*CRGDMFG*CGLLRIHFRIGSRHSRIG
SEQ ID No 4: GG*CRGDMFG*CGG-LFIHFRIGSRHSRIG
SEQ ID No 5: GG*CRGDMFG*CGSLFIHFRIGSRHSRIG
20 SEQ ID No 6: GG*CRGDMFG*CGLLFIHFKIGSRHSRIG
SEQ ID No 7: GG*CRGDMFG*CGLLFIHF^NRIGSRHSRIG
(^NR representing an N-alkylarginine motif)
SEQ ID No 8: GG*CRGDMFG*CGLLSRHFRIGSRHSRIG
SEQ ID No 9: GG*CRGDMFG*CGLLSIHFRIGSRHSRIG
25 SEQ ID No 10: GG*CRGDMFG*CGLLFRHFRIGSRHSRIG.

5. The peptide as claimed in claim 1, characterized in that it contains a sequence
SEQ ID No 11: X-R-G-D-M-F-G-X'
30 exposing the RGD motif via a lactam bridge between the amino acids X (X)-C-O-NH-(X'), X and X' being amino acids such that one bears an acid group and the other bears an amine.

35 6. The peptide as claimed in claim 5, characterized in that it corresponds to the sequences SEQ ID No 12 to SEQ ID No 23:

SEQ ID No 12: GGXRGDMFGX'GLLFIHFRIGCRHSRIG
SEQ ID No 13: GGXRGDMFGX'GLLFIFRIGCRFSRIG

SEQ ID No 14: GGXRGDMFGX'GGLLFIHFRIGSRHSRIG
SEQ ID No 15: GGXRGDMFGX'GGLLRIHFRIGSRHSRIG
SEQ ID No 16: GGXRGDMFGX'GG-LFIHFRIGSRHSRIG
SEQ ID No 17: GGXRGDMFGX'GGS�FIHFRIGSRHSRIG
5 SEQ ID No 18: GGXRGDMFGX'GGLLFIHFKIGSRHSRIG
SEQ ID No 19: GGXRGDMFGX'GGLLFIHF^NRIGSRHSRIG
(^NR representing an N-alkylarginine motif)
SEQ ID No 20: GGXRGDMFGX'GGLLSRHFRIGSRHSRIG
SEQ ID No 21: GGXRGDMFGX'GGLLSIHFRIGSRHSRIG
10 SEQ ID No 22: GGXRGDMFGX'GGLLFRHFRIGSRHSRIG
SEQ ID No 23: GGXRGDMFGX'GGLLFIHFRIGSRHSRIG

7. The peptide as claimed in any one of claims 1 to 6, characterized in that it induces apoptosis in human
15 endothelial cells expressing $\alpha\text{V}\beta 3$ receptors.

8. The peptide as claimed in any one of claims 1 to 7, characterized in that it undergoes endocytosis by human endothelial cells expressing $\alpha\text{V}\beta 3$ receptors,
20 localizes in the mitochondrial compartment, and exerts a mitochondriotoxic effect.

9. A pharmaceutical composition, characterized in that it contains a therapeutically effective amount of
25 at least one peptide as defined in any one of claims 1 to 8, in combination with a pharmaceutically acceptable vehicle.

10. The pharmaceutical composition as claimed in
30 claim 9, characterized in that it is in the pharmaceutical form suitable for its administration by injection, in particular in the form of an injectable solution for intravenous administration.

35 11. The use of peptides as claimed in any one of claims 1 to 8, for producing antiangiogenic medicaments for the treatment of pathologies due to hyper-vascularization.

12. The use as claimed in claim 11, for producing medicaments for the treatment of solid tumors such as pulmonary tumors, adenomas, melanomas, prostate cancer, breast cancer, colon cancer, pancreatic cancer or
5 osteosarcomas, or the treatment of diabetic retinopathies and of arthritis.